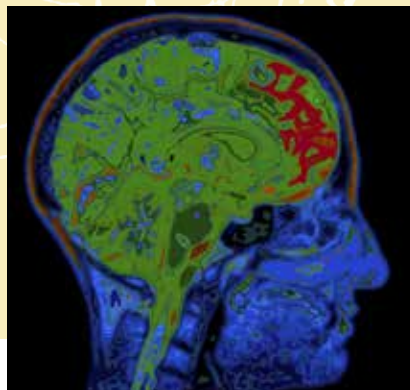


Forum on Neuroscience and Nervous System Disorders

2015 Annual Report



Message from the Chairs

Steven Hyman and Story Landis

Disorders of the nervous system are common, major causes of premature mortality and, in aggregate, the largest cause of disability worldwide. With the vast unmet medical needs associated with these disorders, declining industry investment in brain disorders is cause for concern. The discovery and development of new treatment mechanisms present particular challenges in comparison to other disease areas such as cancer. For example, there are gaps in our understanding of disease mechanisms, a paucity of appropriate animal models to predict efficacy, a lack of biomarkers, and long time horizons for clinical trials. Because our brains undergird cognition, behavior, and personal identity, the application of new technologies such as neurostimulation and brain–computer interfaces raise important ethical, social, and even legal questions concerning culpability. Furthermore, emerging technologies that raise significant ethical issues across all of medicine—including cell transplantation and genome engineering—raise unique considerations as they are applied to the brain.

For 10 years the Forum on Neuroscience and Nervous System Disorders has provided an important venue for candid discussions about emerging and critical issues among key stakeholders, including federal agencies that serve as research sponsors and regulators; the private sector; the academic community; and the nonprofit sector, including foundations and groups focused on nervous system disorders. Through the Forum’s activities, participants have been better able to share information and concerns and to understand each other’s goals and priorities. The dialogue has often yielded ideas for concrete actions or produced new collaborations.

In 2015, discussions addressed a wide range of topics in membership meetings and large public workshops, including the encouragement of greater collaboration across federal agencies supporting aspects of the presidential Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative; the state of financial incentives to encourage research and development of treatments for unmet needs in central nervous system (CNS) disorders; a possible new focus on cognitive dysfunction in depression; the opportunities and challenges related to non-invasive neuromodulation devices; the use of digital health records for Alzheimer’s disease research; and the continuation of efforts to improve mental and neurological health care in the developing world, with a focus this past year on Ghana and Kenya.

Looking ahead to 2016, the Forum plans to address such important topics as improving clinical trial methodology to address CNS disorders; multi-modal therapy approaches that combine drugs, devices, and psychosocial interventions; steps toward an ethical and more robust focus on human biology in therapeutic discovery and development, in recognition of the limitations of animal models in predicting efficacy; steps toward an ethical and more robust focus on human biology in recognition of the limitations of animal models in predicting efficacy; and ethical, legal, and social issues related to emerging neurotechnologies.

We look forward to another year of engaging and productive dialogue.



Steven Hyman
Chair



Story Landis
Vice-Chair

Reflecting Back

Forum Activities in 2015

Financial Incentives to Encourage Development of Therapies That Address Unmet Medical Needs for Nervous System Disorders

The global burden of nervous system disorders is projected to increase significantly over time and is estimated to cost society more than \$6 trillion per year by 2030, according to the 2011 report *The Global Economic Burden of Noncommunicable Diseases* by the World Economic Forum and the Harvard School of Public Health. Despite the market potential and recent international research initiatives to understand the human brain better, many large pharmaceutical companies have decreased investment or even closed their neuroscience research programs based on their judgment of the difficulty of the science and the historically high failure rate of CNS drugs in late-stage clinical trials. As a result, an enormous number of patients remain without effective treatments. The Forum hosted a public workshop to explore policy options that would encourage new private-sector investments and foster innovation in the development of novel therapeutics for nervous system disorders.

Enabling Development, Discovery, and Translation for Cognitive Dysfunction in Depression

Depression is a highly prevalent and disabling disorder. Existing treatments (including both medications and psychotherapies) are only partly effective for some patients and ineffective for many. Often, patients who would be considered responders by clinical trial criteria continue to have symptoms and are unable to return to their previous level of function (e.g., study or work). Increasing clinical and epidemiologic evidence suggests that cognitive dysfunction is an unappreciated aspect of depression that may well contribute to ongoing symptoms and poor functional outcomes. Currently available treatments have only modest benefits in treating cognitive dysfunction in depression, and some treatments, especially

FORUM ACTIVITIES TIMELINE

2006

October 4-5
1st Meeting

2007

February 26
Biomarkers Workshop

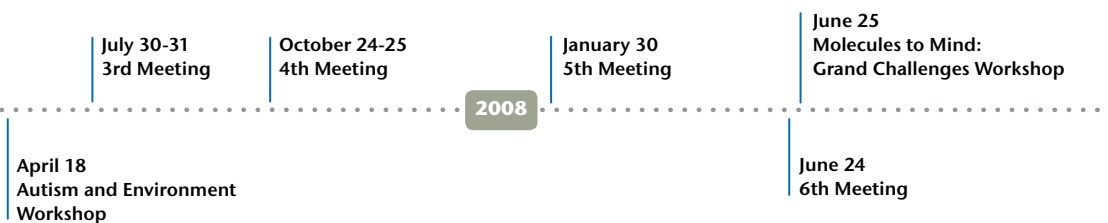
February 27
2nd Meeting



older drugs with anticholinergic properties, may actually worsen cognitive function in some patients. At present, the scientific field has not agreed on the best way to assess cognitive dysfunction in depression or whether this dimension of illness is dependent on, or independent of, mood symptoms. The Forum convened key stakeholders to explore how best to enable the discovery, development, and translation of treatments for cognitive dysfunction in depression, including a focus on the regulatory path forward.

Non-Invasive Neuromodulation of the Central Nervous System

Because of advances in biotechnology and neuroscience, non-invasive neuromodulation devices are of increasing interest to clinicians, patients, health systems, and payers and could acquire significant clinical importance in the coming years. Evidence suggests that both therapeutic and non-clinical applications of non-invasive neuromodulation will continue to expand, particularly where treatments



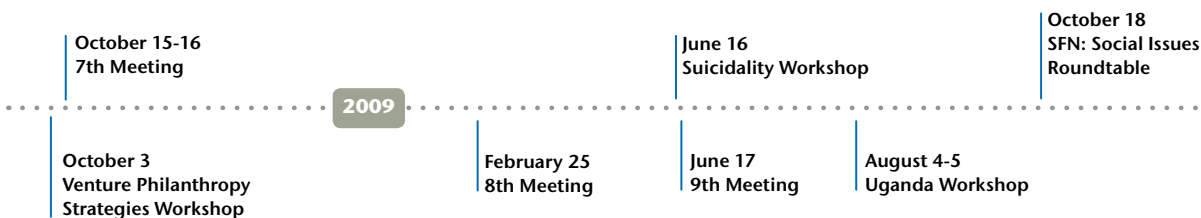
are currently insufficient, such as drug-resistant depression. Along with the growing number of opportunities, there are challenges and open questions regarding scientific understanding of neuromodulation, therapeutic risks and benefits, ethics, regulation, and reimbursement. The Forum hosted a public workshop to explore these questions and identify potential opportunities for additional research and action.

Assessing the Impact of Applications of Digital Health Records on Alzheimer’s Disease Research

Alzheimer’s disease is the most common cause of dementia in older adults, yet no effective therapies are currently available to treat the symptoms or slow the progression of the disease. The Forum hosted a session at the 2015 Alzheimer’s Association International Conference to explore how digital health records might be used to help improve clinical trial design and methodology for Alzheimer’s disease research. The session brought together an international group of experts in translational, epidemiological, and health services research along with an ethicist and representative of a big data analytics company.

Providing Sustainable Mental and Neurological Health Care in Ghana and Kenya

Mental, neurological, and substance use (MNS) disorders are the leading cause of disability and the 10th leading cause of death worldwide. Despite this high burden, there is a significant shortage of resources available to prevent, diagnose, and treat these disorders in low- and middle-income countries. Approximately four out of five people with serious MNS disorders do not receive needed health services, with sub-Saharan Africa having one of the largest treatment gaps. Expanding on previous efforts in sub-Saharan Africa, the Forum, in collaboration with the Academies’ Board on Global Health and African



Science Academy Development Initiative, convened two workshops to examine country-specific opportunities to improve the health care infrastructure in Ghana and Kenya in order to better prevent, diagnose, and treat MNS disorders. Participants in both workshops were asked to identify specific opportunities to advance sustainable access to mental and neurological health care and ensure that the right patients get the right care and treatment at the right time and in the right setting.



November 9
Animal Law
Workshop

March 8-9
Sex Differences
Workshop

June 23
11th Meeting

July 12
ICAD 2010 Session

2010

November 3
10th Meeting

June 22
Glutamate Workshop

December 10
12th Meeting

Looking Forward

Forum Activities in 2016

Neuroscience Trials of the Future

Although major strides have been made over the past two decades in basic neurosciences, the pace of translation into more effective treatments has eluded the field. Among the many factors contributing to this reality is the fact that clinical trial methodology has barely changed, with the possible exception of the increased use of electronic data acquisition and analysis. Better methods, from clinical study design through execution and evaluation, could help enhance the integrity, feasibility, acceptability, efficiency, and economic viability of clinical neuropsychiatric development. The Forum will convene a public workshop to bring together key stakeholders to discuss ways to advance therapeutic development for nervous system disorders by using innovative clinical trial designs; improving patient selection, engagement, and retention; and enhancing clinical monitoring to help decrease the failure rate of drugs and devices in development.



Multimodal Therapies for Nervous System Disorders

Numerous studies have shown that combining therapies of different modalities (e.g., drugs, devices, psychosocial interventions) may be more efficacious than monotherapy for many diseases and disorders. Given the complexity of many conditions, multimodal therapies have the ability to treat different aspects (e.g., chemical and behavioral) of a disease. However, this model has not been used for many brain disorders. The Forum will host a public workshop to explore the utility of multimodal therapies for nervous system disorders, bringing together key stakeholders to consider the opportunities and challenges to the development, regulation, and reimbursement of such approaches.

Therapeutic Development for Nervous System Disorders in the Absence of Animal Models

Although the prevalence and burden of nervous system disorders remains high, development of new therapeutics lags behind other disease areas. Gaps in understanding of the underlying mechanisms of disease and the challenges of using animal models to predict drug efficacy for human brain disorders have contributed to large pharmaceutical companies moving away from neuroscience research programs. Building on previous Forum workshops (Improving the Utility and Translation of Animal Models for Nervous System Disorders [2012] and Accelerating Therapeutic Development for Nervous System Disorders Toward First-in-Human Trials [2013]), the Forum will convene a public workshop to explore additional ways to accelerate early stages of drug development for nervous system disorders. For example, the workshop might explore the possibility of new public-private partnerships to establish biomarkers, learning from the successes and difficulties of the Alzheimer's Disease Neuroimaging Initiative or new diagnostic scales

March 28-29
Animal Models Workshop

July 11
17th Meeting

October 4-5
Sharing Clinical
Research Data Workshop

March 28
16th Meeting

May 10-11
Neurodegeneration
Workshop

September 4-5
SSA Human Resources
Workshop

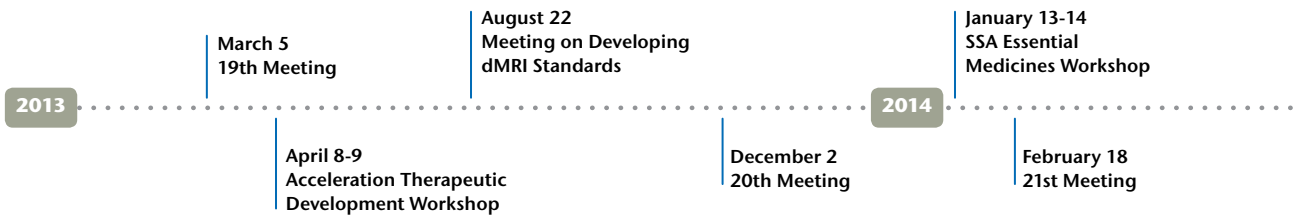
November 18
18th Meeting

for psychiatric symptoms and impairments. The Forum might also build on the prior workshops, which began to consider the evidence needed to bring compounds that appear to be safe into human efficacy trials, even if no predictive animal model has been found.

Responsible Innovation and the Brain—Societal Dimensions of Neurotechnology Advances

Emerging neurotechnologies have the potential to enhance human lives, offering better health outcomes and higher quality of life through the prevention and treatment of mental illness and neurological disease. But the scientific advances that have given rise to these new technologies raise a host of ethical, legal, and social issues. Across the world, large-scale brain initiatives are deepening our understanding of how a healthy brain functions, developing new tools to address open questions in fundamental neuroscience, and deciphering the biological underpinnings of neuropsychiatric diseases. With these efforts will come the potential to manipulate brain function both in illness and in health. There is broad international agreement that ethical considerations should be integrated into brain research.

Although the National Institutes of Health and other federal agencies have begun to consider research programs on ethical, legal, and social issues, to date there have been only limited opportunities to compare approaches across the different national and regional initiatives, jurisdictions, and technologies. The Organisation for Economic Co-operation and Development—with collaboration from the Forum and other organizations internationally—will convene a meeting to share ideas for understanding and addressing the societal implications of new neurotechnologies.





June 17
22nd Meeting

October 28
23rd Meeting

November 15
Dry AMD Workshop

November 16
The Neuroscience of
Gaming Session at SfN

2015

January 13-14
Providing Sustainable Access
to Mental Health Care: Kenya
Workshop

January 20-21
Financial Incentives
Workshop

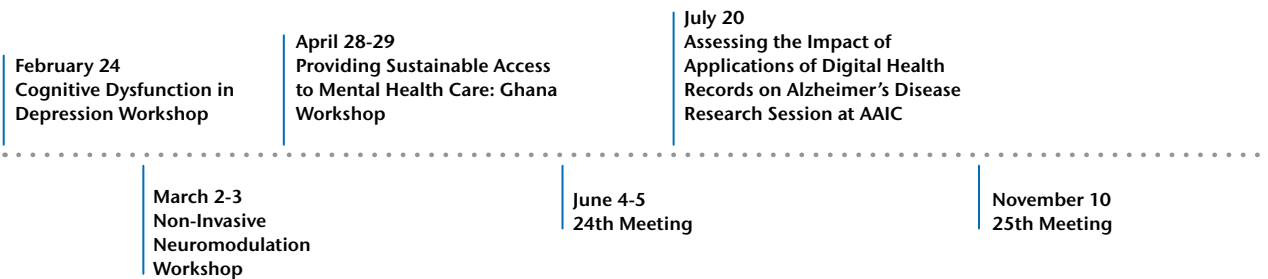
Working Groups

The Forum has working groups to provide additional opportunities to address selected topics. Workshop topics may emerge from these efforts; any such workshops are then organized by an independently appointed workshop planning committee.

Clinical Research Data Sharing

The Forum is participating in an activity on clinical research data sharing that is a collaboration of four Academies forums (focusing on neuroscience; drug discovery, development, and translation; genomics; and cancer). Building on the recent Academies report *Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk*, the group has the following goals:

- **Coordination:** Through communication and organization, improve coordination and collaboration among stakeholders engaged in activities related to data sharing. Contribute to a learning system where stakeholders share information on the outcomes of projects and policies. Provide support and a venue to foster the potential development of a multi-stakeholder body to discuss clinical trial data sharing.
- **Implementation:** Support implementation efforts by creating a mechanism for collaborative participants to identify priority issues and convene or organize other activities where appropriate. Priorities and action items are determined by action collaborative participants and executed by them, with Academies staff support, in their individual/organizational capacities.



Training a Neuroscience Workforce

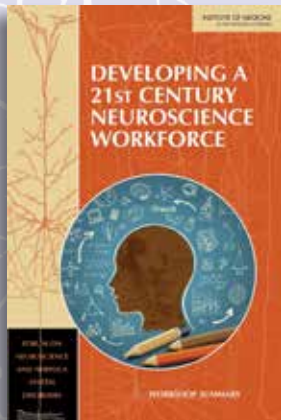
Building on discussions from the 2014 Forum workshop titled Developing a 21st Century Neuroscience Workforce, the Forum established a working group to continue to examine the current challenges and gaps in neuroscience training and identify opportunities to strengthen training programs so that they are tailored to meet the current and future workforce needs.

Mental, Neurological, and Substance Use Disorders in Sub-Saharan Africa

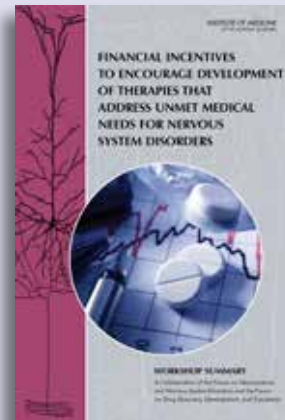
The Forum has a long-standing interest in identifying innovative solutions to enhance care for MNS disorders in sub-Saharan Africa. Since 2009, the Forum has hosted five workshops in Ethiopia, Ghana, Kenya, and Uganda to examine both general and country-specific barriers and potential innovative solutions, with particular focus on increasing human and financial resources to support current and future efforts. Using the World Health Organization Mental Health Gap Action Programme as a basis, the Forum, in collaboration with global entities, is continuing to explore additional opportunities to contribute in this area.



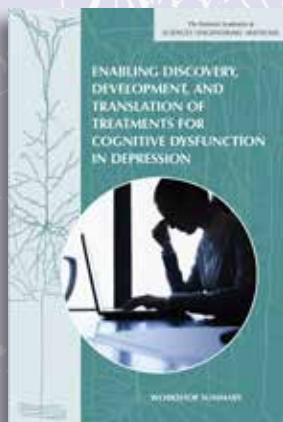
2015 Publications



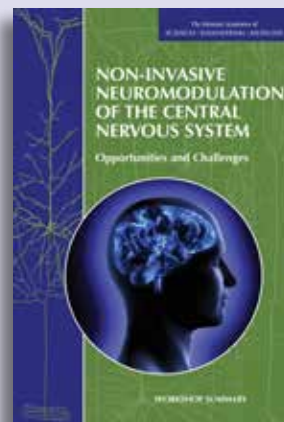
Developing a 21st Century Neuroscience Workforce: Workshop Summary



Financial Incentives to Encourage Development of Therapies That Address Unmet Medical Needs for Nervous System Disorders: Workshop Summary

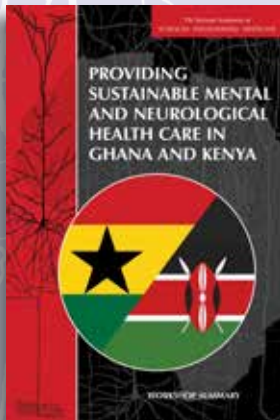


**Enabling Discovery,
Development, and Translation
of Treatments for Cognitive
Dysfunction in Depression:
Workshop Summary**

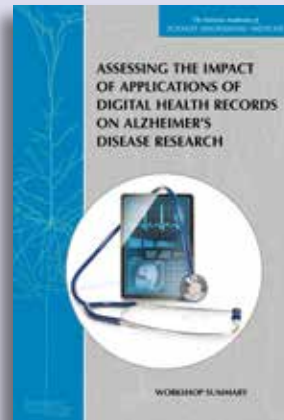


**Non-Invasive Neuromodulation
of the Central Nervous System:
Opportunities and Challenges:
Workshop Summary**

2015 Publications



Providing Sustainable Mental and Neurological Health Care in Ghana and Kenya: Workshop Summary



Assessing the Impact of Applications of Digital Health Records on Alzheimer's Disease Research: Workshop Summary



Advancing Therapeutic Development for Dry Age-Related Macular Degeneration (AMD): Workshop in Brief



The Neuroscience of Gaming: Workshop in Brief

Forum Members

(as of December 2015)

Membership in the Forum includes a diverse range of stakeholders from multiple sectors, including government, the pharmaceutical and biotechnology industries, biomedical research founders and sponsors, academia, and patient groups.

Steven Hyman (Chair)

Broad Institute of the Massachusetts
Institute of Technology and Harvard

Story Landis (Vice-Chair)

Former Director, National Institute of
Neurological Disorders and Stroke

Susan Amara

Society for Neuroscience

Rita Balice-Gordon

Pfizer Inc.

Katja Brose

Cell Press

Daniel Burch

Pharmaceutical Product Development,
Inc.

Sarah Caddick

Gatsby Charitable Foundation

Rosa Canet-Aviles

National Institutes of Health

Maria Carrillo

Alzheimer's Association

C. Thomas Caskey

Baylor College of Medicine

Karen Chandross

Sanofi

Timothy Coetzee

National Multiple Sclerosis Society

Fay Lomax Cook

National Science Foundation

Bruce Cuthbert

National Institute of Mental Health

William Dunn

Food and Drug Administration

Emmeline Edwards

National Center for Complementary
and Integrative Health, NIH Blueprint

Martha Farah

University of Pennsylvania

Daniel Geschwind

University of California, Los Angeles

Hank Greely

Stanford University

Magali Haas

Cohen Veterans Bioscience

Ramona Hicks

One Mind

Richard Hodes

National Institute on Aging

Stuart Hoffman

Department of Veteran Affairs

Michael Irizarry

Eli Lilly and Company

John Isaac

Wellcome Trust

Inez Jabalpurwala

Brain Canada Foundation

Frances Jensen

University of Pennsylvania Health
System

George Koob

National Institute on Alcohol Abuse
and Alcoholism

Walter Koroshetz

National Institute of Neurological
Disorders and Stroke

Alan Leshner

Chief Executive Officer Emeritus,
American Association for the
Advancement of Science

Husseini Manji

Janssen Research & Development, LLC

David Michelson

Merck Research Laboratories

James Olds

National Science Foundation

Atul Pande

Tal Medical

Steven Paul

Voyager Therapeutics

Emiliangelo Ratti

Takeda Pharmaceuticals International,
Inc.

Todd Sherer

The Michael J. Fox Foundation for
Parkinson's Research

David Shurtleff

National Center for Complementary
and Integrative Health

Paul Sieving

National Eye Institute

Nora Volkow

National Institute on Drug Abuse

Stevin Zorn

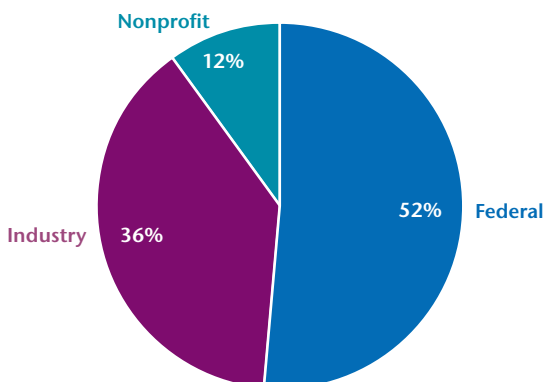
Lundbeck USA

Forum Sponsorship

(as of December 2015)

Financial support for the Forum is derived from federal agencies, disease advocacy organizations, industry, and a nonprofit membership society.

Alzheimer's Association
 Brain Canada Foundation
 Cohen Veterans Bioscience
 Department of Veterans Affairs
 Eli Lilly and Company
 Food and Drug Administration
 Foundation for the National Institutes of Health
 Gatsby Charitable Foundation
 Genzyme, a Sanofi Company
 Janssen Research & Development, LLC
 Lundbeck USA
 Merck Research Laboratories
 The Michael J. Fox Foundation for Parkinson's Research
 National Center for Complementary and Integrative Health
 National Eye Institute
 National Institute of Mental Health
 National Institute of Neurological Disorders and Stroke
 National Institutes of Health Blueprint for Neuroscience Research
 National Institute on Aging
 National Institute on Alcohol Abuse and Alcoholism
 National Institute on Drug Abuse
 National Multiple Sclerosis Society
 National Science Foundation
 One Mind
 Pfizer Inc.
 Pharmaceutical Product Development, Inc.
 Sanofi
 Society for Neuroscience
 Takeda Pharmaceutical Company, Inc.
 Wellcome Trust



About the Neuroscience Forum

The Forum on Neuroscience and Nervous System Disorders at the National Academies of Sciences, Engineering, and Medicine was established in 2006 to bring together government, industry, academia, disease advocacy organizations, and other interested parties. The Forum meets several times per year and provides its members with a structured, neutral venue for exchanging information, ideas, and differing perspectives. At its meetings, the Forum examines significant—and sometimes contentious—issues concerning scientific needs and opportunities, priority setting, and policies related to neuroscience research, its societal implications, and nervous system disorders, and the development, regulation, and use of interventions for the nervous system.

The Forum sponsors workshops (symposia), workshop summaries, and commissioned papers as additional mechanisms for informing its membership, other stakeholders, and the public about emerging issues and matters deserving scrutiny. Information about past and upcoming meetings is available at the Forum's website, www.nas.edu/neuroforum.

Forum Staff

Clare Stroud, Ph.D.

Forum Director

Sheena Posey Norris, M.S.

Program Officer

Joanna Roberts, M.P.P.

Senior Program Assistant

Board on Health Sciences Policy

Andrew M. Pope, Ph.D.

Director

About the National Academies of Sciences, Engineering, and Medicine

The **National Academy of Sciences** was established in 1863 by an Act of Congress, signed by President Lincoln, as a private, nongovernmental institution to advise the nation on issues related to science and technology. Members are elected by their peers for outstanding contributions to research. Dr. Ralph J. Cicerone is president.

The **National Academy of Engineering** was established in 1964 under the charter of the National Academy of Sciences to bring the practices of engineering to advising the nation. Members are elected by their peers for extraordinary contributions to engineering. Dr. C. D. Mote, Jr., is president.

The **National Academy of Medicine** (formerly the Institute of Medicine) was established in 1970 under the charter of the National Academy of Sciences to advise the nation on medical and health issues. Members are elected by their peers for distinguished contributions to medicine and health. Dr. Victor J. Dzau is president.

The three Academies work together as the **National Academies of Sciences, Engineering, and Medicine** to provide independent, objective analysis and advice to the nation and conduct other activities to solve complex problems and inform public policy decisions. The Academies also encourage education and research, recognize outstanding contributions to knowledge, and increase public understanding in matters of science, engineering, and medicine.

Learn more about the National Academies of Sciences, Engineering, and Medicine at www.national-academies.org.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

The nation turns to the National Academies of Sciences, Engineering, and Medicine for independent, objective advice on issues that affect people's lives worldwide.

www.national-academies.org